

# Four-dimensional MR microscopy of the mouse heart using radial acquisition and liposomal gadolinium contrast agent

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## Introduction

Magnetic Resonance Imaging (MRI) has significant potential for evaluating cardiac function in the mouse. However, the majority of work done in mouse cardiac imaging has been with slice-selective techniques, which have a limited Z resolution of 1mm [1,2]. To acquire images that allow the spatial resolution anatomically comparable to clinically acquired images, the resolution along the slice axis must be improved. Reducing the slice thickness decreases the signal-to-noise ratio (SNR), while increasing the number of slices required to cover the entire heart. To address these problems, we propose a 3D plus time radial MRI pulse sequence that allows rapid acquisition of high-resolution cine images at isotropic 87  $\mu\text{m}$  resolution. Mice are injected with liposomal Gd [3], a blood pool contrast agent, allowing 4D acquisition with high contrast and signal-to-noise ratio. High-resolution images allow more sensitive calculation of functional cardiac parameters, e.g. ejection fraction (EF), end-diastolic volume (EDV), end-systolic volume (ESV) and stroke volume (SV), as well as visualization of all 4 cardiac valves and both left and right coronary arteries. This technique represents a factor of 10 improvement in spatial resolution over previously described 2D techniques [1,2] and a factor of 8 improvement over previous 3D techniques [4] with half the acquisition time—31 minutes.

## Methods

10 C57BL/6J mice were anesthetized using isoflurane and were allowed to breathe freely throughout the study. A long circulating Gadolinium liposomal blood pool contrast agent (CE-Gd) [3] was used to increase the signal and contrast-to-noise ratio between the blood and the myocardium. The contrast agent was administered intravenously at a dose of 0.2 mmol Gd/kg resulting in an average injection of 0.10 mL for a 21-gram mouse. Temperature, heart rate, and breathing rate were monitored using ECG equipment developed by SA Instruments (Edison, NJ USA) and kept as consistent as possible throughout the scan.

All work was performed at 7T with a GE EXCITE console (EPIC 12.4). A 4D radial MRI pulse sequence was implemented and optimized to reduce echo time (TE) and repetition time (TR) to 300  $\mu\text{s}$  and 2.4 ms respectively, to increase temporal resolution and reduce scan time by allowing for multiple views to be acquired for each heart beat. The sequence was cardiac gated, but not ventilatory gated, and consisted of center-out trajectories (Figure 1a). In order to decrease phase artifacts in reconstructed images, view order acquisition was randomized (Figure 1b). Eight phases of the heart cycle were acquired at a temporal resolution of 9.6ms and at a spatial resolution of 87 x 87 x 87 microns in 31 minutes. Images were imported into ImageJ and the left ventricle was threshold segmented for each phase of the heart cycle to measure EDV, ESV, SV, and EF.

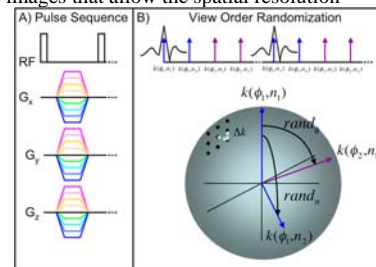
## Results and Discussion

Figure 2 shows the 8 phases of the heart cycle for a representative mid-ventricle short-axis plane (top) and the long-axis plane (bottom) for the same dataset. Isotropic resolution allowed arbitrary orientation of the plane permitting visualization of all four heart valves, as well as the left coronary artery. A 4-chamber heart view along with visualization of the 4 heart valves and coronary arteries can be seen in Figure 3.

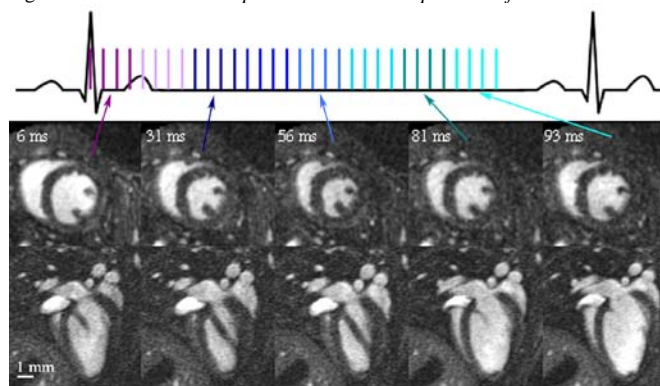
3D high-resolution images allow more sensitive calculations of cardiac function. The high SNR and CNR of the 87x87x87  $\mu\text{m}$  arrays allow easy segmentation of the left ventricle for each phase of the heart cycle. Unlike traditional slice-selective bright blood images [5], no flow voids are seen allowing more accurate segmentation. For the 10 C57BL/6J mice used in this study, with an average weight of  $26.3 \pm 1.8\text{g}$ , the EDV was  $65.26 \pm 7.40 \mu\text{L}$ , the ESV was  $26.86 \pm 2.24 \mu\text{L}$ , the SV was  $38.40 \pm 5.93 \mu\text{L}$ , the cardiac output was  $18.00 \pm 3.10 \text{mL/min}$ , and the EF was  $58.64 \pm 2.83\%$ . The values reported closely match the values reported in other work [6]. This method presents an excellent alternative for functional cardiovascular phenotyping of the mouse heart as it is non-invasive (thus allowing the potential for longitudinal studies), and has a reasonable acquisition time of 31 minutes.

**References:** 1) Zhou, R. et al. MRM 49(4):760-764, 2003. 2) Cassidy, P.J. et al. JMRI 19(2):229-237. 3) Ghaghada, K. et al. Am J Neuro 28(1):48-53, 2007. 4) Fientuch, A. et al. NMR Biomed 20:360-265,2007. 5) Berr, S. et al. MRM 53:1074-1079, 2005. 6) Badea, C. et al. Mol Imag 4(2):110-116, 2005.

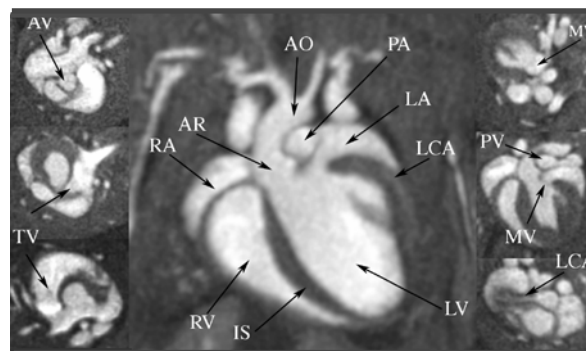
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**Figure 1:** 4D radial pulse sequence implemented on a 7T GE Signa scanner (A), as well as view order randomization scheme (B) implemented to reduce phase artifacts.



**Figure 2:** 5 representative heart phases (out of a total of 8 phases acquired) are shown in both short-axis view (top row) and long-axis view (bottom row). Images were acquired with a resolution of 87x87x87 microns in 31 minutes and a temporal resolution of 9.6ms.



**Figure 3:** High-resolution images result in ability to visualize the leaflets of all 4 heart valves as well as left coronary artery. Four-chamber view shows right atria (RA), left atria (LA), left ventricle (LV), right ventricle (RV), interventricular septum (IS), left coronary artery (LCA), aortic arch (AO), pulmonary artery (PA), aortic root (AR), mitral valve (MV), aortic valve (AV), tricuspid valve (TV), and pulmonary valve (PV).